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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,930	04/12/2004	Dario Neri	ELLIS-0002-P02-C01	3681

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EXAMINER	
PORTNER, VIRGINIA ALLEN	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
07/12/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@mwzb.com

Office Action Summary	Application No.	Applicant(s)	
	10/821,930	NERI ET AL.	
	Examiner	Art Unit	
	GINNY PORTNER	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2010 and 07 May 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-26,28-34 and 36-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-26,28-34 and 36-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *4/5/2010* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/7/2010; 4/5/2010;3/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 19-26, 28-34, 36-45 are pending.

Rejections Withdrawn

1. The rejection of Claims 19, 20, 36 under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter is herein withdrawn in upon further consideration of the subject matter claimed in the instant Application and the issued claims of US Pat. 7,129,254, SEQ ID NO 1.
2. The rejection of claims 19-20, 36,39-42, 44-45 under 35 U.S.C. 102(g) based upon claims 1, 9 and 14 of Patent No. 7,129,254 is herein withdrawn in upon further consideration of the subject matter claimed in the instant Application and the issued claims of US Pat. 7,129,254, SEQ ID NO 1.
3. The obviousness type double patenting rejection over copending application 10/336,041 is herein withdrawn.

Information Disclosure Statement

1. The information disclosure statement filed May 7, 2010 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

- References", C12 "Chen et al" and C35 ' Kim et al" could not be found among the submitted references, nor cited on any prior US PTO 1449, and therefore were cited but not provided for consideration.
- Cover sheet submitted for reference WO95/32001(provided coversheet, but not reference); No explanation of relevance provided for either citation

.

Response to Amendment

1. The Amendment to the Specification submitted April 5, 2010 does not comply with 37 CFR 1.121 for the following reasons:

2. The amendment of the Specification submitted **4/5/2010** which sought to amend the header of Table 1 can not be entered because the current Table 1, which was original Table 2 (Amended Specification 3/10/2009), does not set for columns with the recited labels for the amendment of Table 1 dated April 5, 2010. (see history of Applicant's Amendment(s) below)

Please delete the header for Table 1 and replace it with the following header:

Table 1:

Sequences of selected anti-ED-B antibody clones. The column labeled "50-54*" discloses SEQ ID NOS 27, 27, 27, 28 and 28, respectively, in order of appearance. The column labeled "95-98*" discloses SEQ ID NOS 29, 30, 31, 31 and 31, respectively, in order of appearance. The column labeled "91-96*" discloses SEQ ID NOS 32, 33, 34, 34 and 34, respectively, in order of appearance.

- Amendment of 10/821,930 Specification date **3/10/2009**

Page 34, please delete in its entirety.
The original Table 1 was deleted. Original Specification pg 34 Table 1, filing date 4/12/2004 was deleted.

Applicant chose to renumber original Table 2 as Amended Table 1:

- Pages 35 - 39, please renumber to pages 34 - 38.

Renumbered page 34, first line, please replace with the following: --Table 1~~2~~:--.

Original page 35 (below) was Renumbered to be page 34 in light of Applicant's **of 3/10/2009** amendment (cited above).

~~35~~ 34
"

Table ~~2~~ 1:
Affinities Of anti-ED-B scFv fragments

Clone	kon ($s^{-1}M^{-1}$)	koff (s^{-1})[B]	koff (s^{-1})[C]	K_d (M)*
A2	1.5×10^5	2.8×10^{-4}	-	1.9×10^{-9}
C4	4.0×10^5	3.5×10^{-4}	-	8.7×10^{-9}
E3	1.6×10^5	6.5×10^{-4}	-	4.1×10^{-9}
H10	6.7×10^4	5.6×10^{-4}	9.9×10^{-3}	1.3×10^{-8}
L19	1.1×10^5	9.6×10^{-5}	6.0×10^{-4}	5.4×10^{-21}

*) $K_d = k_{off} / k_{on}$. For the high-affinity binders H10 and L19, k_{off} values from BIAcore experiments are not sufficiently reliable due to effects of the negatively-charged carboxylated solid dextran matrix; Kd values are therefore calculated from k_{off} measurements obtained by competition experiments (Experimental Procedures).
k_{on}, kinetic dissociation constant; k_{on}, kinetic association constant; K_d, dissociation constant. B = measured on the BIAcore; C = measured by competition with electrochemiluminescent detection. Values are accurate to +/- 50%, on the basis of the precision of concentration determinations.

- At page 4, the term " 32", third line from bottom of page, is not underlined showing the change of the prior amendment dated March 10, 2009 which changed the term "32" to ---33--.

- Additionally, the Amendment of the Specification dated April 5, 2010, which sought to amend the Specification to incorporate by reference to a sequence listing that deletes the amino acid sequence of the original L19 linker, SEQ ID NO 20, introduces New Matter into the Specification and therefore is not entered. **Response to Applicant's Overview Remarks**

Please Note: At NO time did the Office state that the originally filed Specification disclosed sequence errors in the disclosed antibody L19 as shown in original Figure 6 as alleged by Applicant. All of the amino acid sequences for the linker for L19 contain a 14 amino acid linker

as originally filed (see original figure 6). The amino acid sequences for both the VH and VL chains are identical in all of the Applications to which the instant Application claims priority:

VH

E V Q L L E S G G G L V Q P G G S L R L S C A A S G F T F S
S F S M S W V R Q A P G K G L E W V S S I S G S S G T T Y Y
A D S V K G R F T I S R D N S K N T L Y L Q M N S L R A E D
T A V Y Y C A K P F P Y F D Y W G Q G T L V T V S S

linker

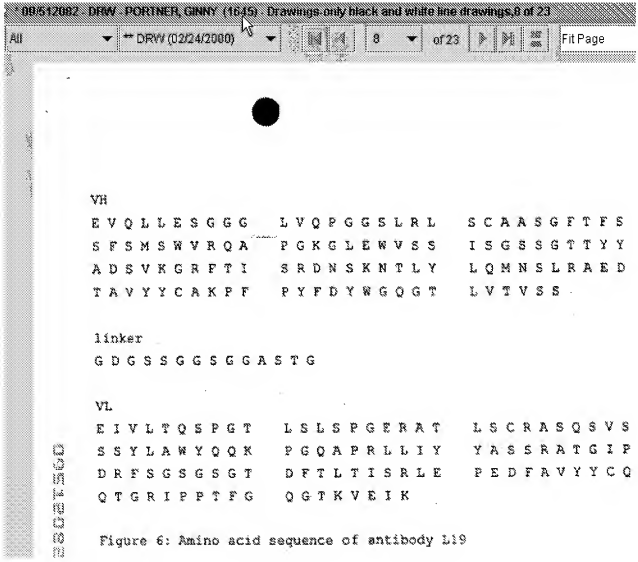
G D G S S G G S G G A S T G

VL

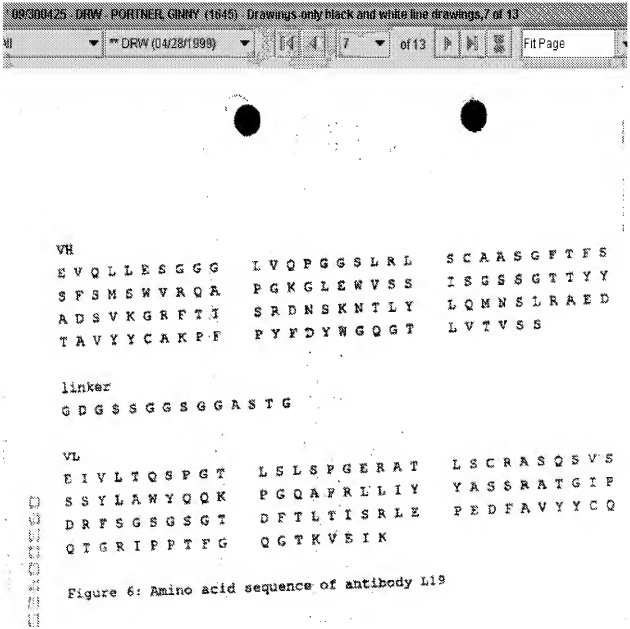
E I V L T Q S P G T L S L S P G E R A T L S C R A S Q S V S
S S Y L A W Y Q Q K P G Q A P R L L I Y Y A S S R A T G I P
D R F S G S G S G T D F T L T I S R L E P E D F A V Y Y C Q
Q T G R I P P T F G Q G T K V E I K

Figure 6: Amino acid sequence of antibody L19

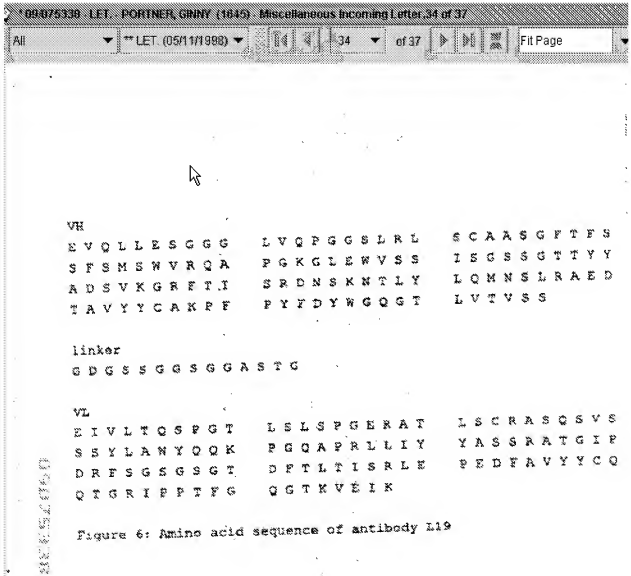
The parent Application 09/512,082 (filed 2/24/2000) also contained the same figure and amino acid sequence, see below:



Grandparent application 09/300425 (filed 4/28/1999) also discloses the same amino acid sequence in Figure 6:



Great-Grandparent Application 09/075,338 (filed May 11, 1998) also disclosed the same amino acid sequence for the L19 Antibody:



Responses to Overview Remarks and Lundak Declaration for Deposit

1. Applicant and the Neri Declaration point to Example 2 of the instant Specification for support for the production of an L19 antibody with only a 12 amino acid linker.

2. Upon further consideration of Example 2 of the originally filed Specification, the Examiner found that L19 was produced by affinity maturation starting from ScFv(E1) (page 22, line 8) into which mutations at locations 31-33 and 50,52 and 54 of the VH chain were introduced.

Example 2 paragraphs are reproduced below:

3. Page 22, lines 8-16: "ScFv(E1) was selected to test the possibility of improving its affinity with a limited number of mutations of CDR residues located at the periphery of the antigen binding site (Figure IA). We combinatorially mutated residues 31-33, 50, 52 and 54 of the antibody VH, and displayed the corresponding repertoire on filamentous phage. These residues are found to frequently contact the antigen in the known 3D-structures of antibody-antigen complexes. The resulting repertoire of 4×10^8 clones was selected for binding to the ED-B domain of fibronectin. After two rounds of panning, and screening of 96 individual clones, an antibody with 27-fold improved affinity was isolated (H10; Tables 1 and 2)."

4. Page 23, lines 1-30: "Affinity maturation experiments were performed as follows. The gene of scFv(E1) was PCR amplified with primers LMBlbis (5'-GCG GCC CAG CCG GCC ATG GCC GAG-3') and DP47CDR1for (5'-GA GCC TGG CGG ACC CAG CTC ATM NNM NNM NNGCTA AAG GTG AAT CCA GAG GCT G-3') to introduce random mutations at positions 31-33 in the CDR1 of the VH (for numbering: 28), and with primers DP47CDR1back

(5'-ATG AGC TGG GTC CGC CAG GCT CC-3') and DP47CDR2for (5'-GTC TGC GTA GTA "IGT GGT ACC MNN ACT ACC MNN AAT MNN TGA GAC CCA CTC CAG CCC CTT-3') to randomly mutate positions 50,52,54 in CDR2 of the VH. The remaining fragment of the scFv gene, covering the 3'- portion of the VH gene, the peptide linker and the VL gene, was amplified with primers DP47CDR2back (5'-ACA TAC TAC GCA GAC TCC GTG AAG-3') and JforNot (5'-TCA TTC TCG ACT TGC GGC CGC TTT GAT TTC CAC CTT GGT CCC TTG GCC GAA CG-3') (94C 1 min, 60 C 1 min, 72 C 1 min); The three resulting PCR products were gel purified and assembled by PCR (21)with primers LMBlbis and JfOrNot (94°C 1 minl 60 C 1 min, 72 C 1 min). The resulting single PCR product was purified from the PCR mix, double digested with NotI/NCol and ligated into NotI/NcoI digested pDN332 vector. Approximately 9 pg of vector and 3 ug of insert were used in the ligation mix, which was purified by phenolisation and ethanol precipitation, resuspended in 50 ul of sterile water and electroporated in electrocompetent TGI E.coli cells. The resulting affinity maturation library contained $4x10^8$ clones. Antibody-phage particles, produced as described (Nissim et al. (1994). EMBO J., 13, 692-698) were used for a first round of selection on 7B89 coated imunotube (Carnemolla et al. (1996). Int. J. Cancer, 68, 397-405). The selected phages were used for a second round of panning performed with biotinylated ED-B, followed by capture with streptavidin coated magnetic beads (Dynal, Oslo, Norway; see previous paragraph). After selection, approximately 25% of the clones were positive in soluble ELISA (see previous chapter for experimental protocol). From the candidates positive in ELISA, we further identified the one (H10; Table 1)with lowest koff by BIAcore analysis (Jonsson et al. (1991), BioTechniques, 11,620-627)."

5. From the above set of clones Scfv (H10) was selected (page 23, line 31, page 22, line 16), and mutations at positions 32 and 50 of the VL light chain were introduced into scFv(H10) in order to obtain the resultant L19 antibody:

Page 22, lines 23-31:

Casterman et al. (1993). Nature, 363, 446-448). For this reason we chose to randomise only two residues (32 and 50) of the VL domain, which are centrally located in the antigen binding site (Figure 1a) and often found in 3D structures to contact the antigen. The resulting library, containing 400 clones, was displayed on phage and selected for antigen binding. From analysis of the dissociation profiles using real-time interaction analysis with a BIAcore instrument (Jonsson et al. (1991). BioTechniques, 11, 620-627) and koff measurements by competition experiments with electrochemiluminescent detection a clone (L19) was identified, that bound to the ED-B domain of fibronectin with a Kd = 54 pM (Tables 1 and 2).

❖ Applicant's response of March 10, 2009 at page 13, lines 5-7, indicates that the post filing deposit of L19 differs by one amino acid in the VL domain and by omission of "TG" in the linker sequence.

❖ Example 2 of the originally filed Specification does not describe nor teach the deletion of 2 amino acids in the linker present in the E1, H10 or L19 antibodies. L19 has the same linker as E1 and H10, the 14 amino acid linker evidencing original descriptive support in the instant Specification in originally filed figure 6 and original claim 10 shown immediately below:.

10. The antibody according to claim 1 with the following amino acid sequence:

VH

EVQLLESGGG LVQPGGSLRL SCAASGFTFS
SFSMSWVRQA PGKGLEWVSS ISGSSGTTYY
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED
TAVYYCAKPF PYFDYWGQGT LVTVSS

linker

GDGSSGGSGGASTG

VL

EIVLTQSPGT LSLSPGERAT LSCRASQSVS
SSYLAWYQQK PGQAPRLLIY YASSRATGIP
DRFSGSGSGT DFTLTISRLE PEDFAVYYCQ
QTGRIPPTFG QGTKVEIK

Example 2 in the instant Specification does not teach, nor describe methods steps for the deletion of any amino acids in the linker of any of the affinity matured antibodies described therein. Nothing in Example 2 of the originally filed Specification supports the post filing date Deposited Antibody coding sequence that contains two less amino acids in the linker and a change in amino acid sequence in the VL chain because Example 2 does not teach nor provide guidance for changing the linker from the 14 amino acids present in E1 or H10 or L19.

It was also noted that the genetic coding sequences for scFv antibodies E1, H10 and L19 were recorded in EMBL May 12, 1998 by Viti, a common inventor of the instant invention, the day after the filing date of great-grandparent application (09/075,338, filed May 11, 1998) to which the instant Application claims priority and all three coding sequences for these antibodies encoded a 14 amino acid linker that ended in the amino acids "TG" (EMBL accession numbers (AJ006111; AJ006112; AJ006113) corresponding to Swiss-Prot accession numbers (A2KBB9,A2KBCO,A2KBC1(text file dated Feb. 20, 2007), respectively).

In light of Applicant's Representatives Remarks, dated March 10, 2009, at page 13, lines 5-7, that the post filing deposit of L19 differs by one amino acid in the VL domain and by omission of "TG" in the linker sequence, Applicant admits on the record that the amino acid sequence encoded by the DNA in the Deposit ATCC deposit no. PTA-9529 does not correspond to that described in the parent applications at the time of filing and produced by the method of Example 2. As such, the recitation of the Deposited material in the claims and the Specification constitutes New Matter.

Applicant's "Lundack" Declaration submitted April 5, 2010 does not address this apparent discrepancy on this record. Applicant's description of the deposited material containing sequencing errors is inconsistent with its' method of making in Example 2. It is again noted that the product from which L19 of the Specification was derived has a 14 amino acid linker.

Applicant indicated that L19 actually has a 12 amino acid linker but there is no method steps indicated in the method of affinity maturation of Example 2 that accounts for this discrepancy. It is the position of the Office that the material deposited as ATCC deposit no. PTA-9529, DNA that encodes L19, was admitted to lack 2 amino acids in the linker sequence, this linker sequence lacks written description in the Specification as originally filed. Therefore the later deposited material does not have original descriptive support and as such constitutes New Matter. The Lundak declaration does not address this issue. The Lundak Declaration swears that the L19 is that described by Example 2, and therefore not persuasive on its face given the inconsistency on this record.

6. It is noted that Applicant has obscured this issue by deleting the material describing the L19 antibody as original filed. Applicant has deleted the amino acid sequence for the linker and

VL chain for the sequence listing and Figure 6 (original SEQ ID No 20 and 21). Seq. ID Nos. 20 and 21 have been deleted and now recite "000" (submitted 4/5/2010) instead of the originally filed sequences (filed 4/12/2004).

Objections and Rejections Maintained

4. The New Matter rejection of the claims 19-26, 28-34, 36-45 under 35 USC 112, first paragraph (written description, new matter) and the objection to the Specification under 35 U.S.C. 132(a) due to the amendment filed March 10, 2009 because it introduces New Matter into the disclosure is maintained for reasons of record and responses set forth herein. The only scFv antibody the instant Specification provides original descriptive support for that comprises SEQ ID NO 19 (VH domain) is the Deposited antibody encoded by ATCC deposit no. PTA-9529, therefore all of the pending claims have been included in the New Matter rejection; the rejection is maintained for reasons of record and responses set forth herein.

Applicant states that the L19 antibody has been deposited into a repository and the specification has been amended to include the deposit information. Applicant has failed to provide the statement that that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application. Until this statement is made Applicant have not satisfied all the conditions of 37 CFR 1.801-1.809 and Applicant has not established possession for the isolated antibody, L19 disclosed in the specification

5. In response to the rejection of claim 28 under 35 U.S.C. 112, first paragraph (New Matter), as failing to comply with the written description requirement. The claim(s) contains

subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention Applicant states claim 28 has been canceled.

6. Claim 28 has **not** been cancelled, therefore the rejection is maintained for reasons of record.

7. The objection to claim 24 because of the informalities was not resolved by Applicant's claim amendment as claim 24 still recites the term "chlorine", but should be amended to recite----chlorin-----. The objection is maintained for reasons of record.

Double Patenting

8. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. The rejection of claims 20 and 25 provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 42 and 44 of copending Application No. 10/321,558 is traversed on the grounds that copending Application 10/321,558 is directed to antibodies *per se*.

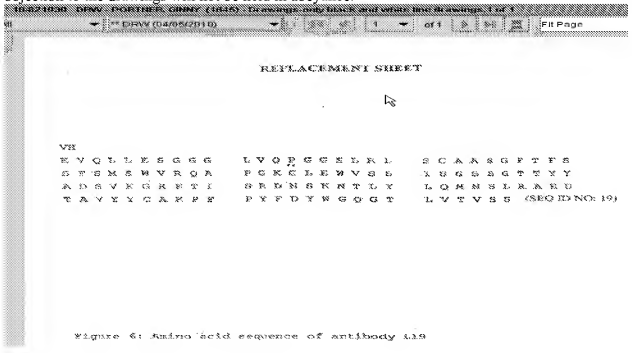
11. In response to Applicant's statement, the examiner would like to point out that Application 10/321,558 claim 44, which depends from claim 42, is directed to an antibody conjugate, specifically a radiolabeled antibody, which is the same invention as instant claim 25 which depends from independent claim 20 and is directed to an antibody conjugate of a radionuclide. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

New Grounds of Objection/Rejection Necessitated by Amendment

Drawings

2. The drawings are objected to under 37 CFR 1.83(a) because they fail to show the entire L19 antibody as described in drawing Figure 6 and specification. Replacement sheet submitted April 5, 2010 is labeled "Figure 6: Amino acid sequence of Antibody L19", but only shows the VH domain. Antibody L19 contains a VH domain, a VL domain and a 14 amino acid linker. Figure 6 does not show what the figure is labeled. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing

should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.



Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 19, 20, 25-26, 29, 44-45 are provisionally rejected

"Claim 19. (Currently amended) A method for diagnosis or therapy of tumours or a vascular proliferation disease in a patient ~~comprises comprising~~ administering an antibody with specific, high affinity for the ED-B domain of fibronectin having a VH domain with the following amino acid sequence:

VH domain (SEQ ID NO: [[30]]19)

EVQLLESGGG LVQPGGSLRL SCAASGFTFS SFSMSWVRQA PGKGLEWVSS

ISGSSGTTYY ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKPF

PYFDYWGQGTLVTVSS and having a VL domain with the amino acid sequence encoded by the VL domain encoding DNA of the DNA insert of ATCC deposit no. PTA-9529.

Claim 20. (Currently amended) A conjugate comprising (a) an antibody with specific, high affinity for the ED-B domain of fibronectin having a VH domain with the following amino acid sequence: VH domain (SEQ ID NO: [[30]]19) EVQLLESGGG LVQPGGSLRL SCAASGFTFS SFSMSWVRQA PGKGLEWVSS ISGSSGTTYY ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKPF PYFDYWGQGTLVTVSS and having a VL domain with the amino acid sequence encoded by the VL domain encoding DNA of the DNA insert of ATCC deposit no. PTA-9529; and (b) a molecule capable of inducing blood coagulation and blood vessel occlusion.

Claim 25. (Previously Presented) A conjugate according to claim 20 wherein the molecule capable of inducing blood coagulation and blood vessel occlusion is a radionuclide.

Claim 26. (Previously Presented) A conjugate according to claim 25 wherein the radionuclide is a B-emitting radionuclide."

"Claim 29. (Previously Presented) A method for the treatment of an angiogenesis-related pathology in a patient comprising administering a conjugate according to claim 20. "

- on the ground of nonstatutory double patenting over claims 4,17,21-22 of copending Application No. **10/204,581** (cited on US PTO 1449, reference C92, two common inventors Neri and Tarli).

"4.(Previously Presented) A conjugate of (i) a specific binding member specific for an fibronectin ED-B, and (ii) a molecule which exerts a biocidal or cytotoxic effect on target cells by cellular interaction, wherein the specific binding member has at least one of the following characteristics: (i) comprises at least one of the VH domain and the VL domains of antibody L19; (ii) competes with antibody having at least one of the VH domain and the VL domain of antibody L19 for binding to fibronectin ED-B. "

"17. (Previously Presented) A conjugate according to claim 4 wherein the specific binding member is a single-chain. "

"21. (Previously Presented) A method of treatment of angiogenesis in pathological lesions in a patient in need of said treatment, the method comprising administering a conjugate according to claim 4.

22. (Previously Presented) A method according to claim 21 wherein said pathological lesion is a tumor. "

5. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: see copied claims above; Application 10/204, 581 claims a genus of L19 antibodies and method of treatment that includes the instantly claimed antibody and method of treatment. The instant claims being an obvious species within the claimed genus in application 10/204, 581.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Conclusion

1. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on May 7, 2010 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GINNY PORTNER whose telephone number is (571)272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert B Mondesi/
Supervisory Patent Examiner,
Art Unit 1645

/Ginny Portner/
Examiner, Art Unit 1645
June 24, 2010